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(71) 出願人;および

(72) 発明者

輕部征夫(KARUBE, Isao)[JP/JP]

〒216-0002 神奈川県川崎市宮前区東有馬一丁目3番16号 Kanagawa (IP)

Kanagawa, (JP)

齋藤 敬(SAITOH, Takashi)[JP/JP]

〒116-0013 東京都荒川区西日暮里一丁目42番2-1002号

ライオンズマンション西日暮里第2 Tokyo, (JP)

(74) 代理人

弁理士 清水初志, 外(SHIMIZU, Hatsushi et al.)

〒300-0847 茨城県土浦市卸町1-1-1

関鉄つくばビル6階 Ibaraki, (JP)

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添付公開書類

国際調査報告書

(54)Title: APPARATUS FOR AUTOMATICALLY MEASURING MINUTE MEMBRANE POTENTIAL

(54)発明の名称 自動微小膜電位計測装置

(57) Abstract

An apparatus for automatically measuring minute membrane potential, based on a technique developed for controlling a membrane denaturation reaction without using a physical shearing force, for example, a method of causing the destruction of membrane at a limited portion of a living membrane by making a stimulus, such as light and a compound activated by the stimulus react with each other in a membrane, such as a living membrane, this method being applied to a minute electrode to facilitate the insertion thereof into a cell, which has been difficult in the use of a minute metal electrode, and enable membrane potential in a cell to be measured easily, the minute metal electrode enabling the integration thereof and the development of a neural interface in the barrier-free technology.

A ... STIMULUS

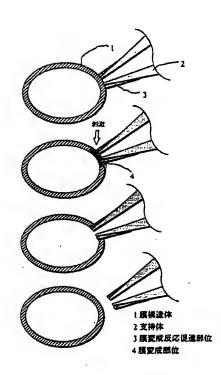
1 ... MEMBRANE STRUCTURE

2 ... SUPPORT MEMBERS

3 ... MEMBRANE DENATURATION REACTION PROMOTING

PORTIONS

4 ... DENATURED PORTION OF THE MEMBRANE





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(12) United States Patent Karube et al.

(10) Patent No.:

US 6,537,800 B1

(45) Date of Patent:

Mar. 25, 2003

(54) APPARATUS FOR AUTOMATICALLY MEASURING MINUTE MEMBRANE POTENTIAL

(75) Inventors: Isao Karube, Kanagawa (JP); Takashi Saitoh, Tokyo (JP)

(73) Assignee: Center for Advanced Science and Technology Incubation, Ltd., Tokyo

(JP)

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(56) References Cited

PUBLICATIONS

Saito et al. 'Light does and time dependency of photodynamic cell membrane damage.' Photochemistry and Photobiology. vol. 68 (1998) No. 5, pp. 745-748.* Robinson, D. A., "The Electrical Properties of Metal Micro-

electrodes," Proceedings of the IEEE, 56:1065–1071 (1968).

Hamill, O. P., et al., "Improved Patch-Clamp Techniques for High-Resolution Current Recording from Cells and Cell-Free Membrane Patches," *Pflügers Archiv*, 391:85–100 (1981).

Kurata S., et al., "The Laser Method for Efficient Introduction of Foreign DNA into Cultured Cells," *Experimental Cell Research*, 162:372–378 (1986).

Valenzeno, D. P., "Photomodification of Biological Membranes with Emphasis on Singlet Oxygen Mechanisms," *Photochemistry and Photobiology*, 46:147–160 (1987).

Horn, R., et al., "Muscarinic Activation of Ionic Currents Measured by a New Whole-Cell Recording Method," *J. Gen. Physiol.*, 92:145–159 (1988).

Levitan, E. S., et al., "Neuropeptide Modulation of Single Calcium and Potassium Channels Detected with a New Patch Clamp Configuration," *Nature*, 348:545–547 (1990). Bard, A. J., et al., "Chemical Imaging of Surfaces with the Scanning Electrochemical Microscope," *Science*, 254:68–74 (1991).

(List continued on next page.)

Primary Examiner—William H. Beisner (74) Attorney, Agent, or Firm—Nixon Peabody LLP

(57) ABSTRACT

An apparatus for automatically measuring minute membrane potential, based on a technique developed for controlling a membrane denaturation reaction without using a physical shearing force, for example, a method of causing the destruction of membrane at a limited portion of a living membrane by making a stimulus, such as light and a compound activated by the stimulus react with each other in a membrane, such as a living membrane, this method being applied to a minute electrode to facilitate the insertion thereof into a cell, which has been difficult in the use of a minute metal electrode, and enable membrane potential in a cell to be measured easily, the minute metal electrode enabling the integration thereof and the development of a neural interface in the barrier-free technology.

13 Claims, 16 Drawing Sheets

SiO₂ (THICKNESS 100 nm)

TOP SURFACE

Au (THICKNESS 220 nm)

SiO₂ (THICKNESS 100 nm)

BOTTOM SURFACE (MEASURING SURFACE)